REMARKS

Claims 24 and 30 are pending in the present application. Claim 31 is added herein for clarity and to more particularly define the invention. Support for new claim 31 can be found in claim 24 as filed as well as on page 5, lines 12-22 of the specification. It is believed that no new matter has been added by these amendments. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application, entry of the new claims and allowance of the claims to issue.

I. Objection to the Specification

The Office Action states that this application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b) and that an abstract on a separate sheet is required.

An Abstract, on a separate sheet, as required by C.F.R. § 1.72(b), is attached hereto. Therefore, applicants believe this objection has been overcome and respectfully request its withdrawal.

II. Rejections Under 35 USC §112, second paragraph

The Office Action states that claims 24 and 30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Office Action, the claims are allegedly vague and indefinite because it cannot be determined how the compound, the cellular gene comprising SEQ ID NO: 75, and the gene product that is necessary for viral replication, but not for cell survival are related to one another. Evaluation of the effectiveness of the compound is measured by detecting the level of activity or decrease of the gene product. If the addition of the compound only affects the gene product, what is the relationship between the gene product and SEQ ID NO: 75 and the compound? The claims also state that the cell contains a cellular gene that comprises SEQ ID NO: 75. Is SEQ ID NO: 75 native to the genetic makeup of the cell or is the sequence transfected? It cannot be determined if SEQ ID NO: 75 is an unisolated natural product or not. Claim 30,

step d) states that the level of viral infection is "associated" with the cellular gene, but it is unclear what the association is or how it is made. The Office Action also states that the metes and bounds of what would be considered a homolog of SEQ ID NO: 75 cannot be determined.

Applicants respectfully point out to the Examiner that the present invention was the first to show that cellular genes involved in viral infection can be identified by utilizing a novel gene trap method. As described in the specification, in order to identify and isolate nucleic acids from genes associated with a particular function, i.e. viral infection, one of skill in the art would transfer a vector encoding a selective marker gene lacking a functional promoter into a cell culture that is growing in serum-containing medium. The skilled artisan would then select cells expressing the marker gene and remove serum from the culture medium. The cells would then be infected with a virus. Many of the cells will not survive viral infection, but those cells containing a vector encoding a selective marker gene that has inserted itself in a cellular gene necessary for viral replication but not necessary for survival of the cell will survive. One of skill in the art can then identify a gene necessary for viral growth in a cell and nonessential for cellular survival in those cells which survived (see page 5, lines 12-17). By utilizing this methods applicants have identified over one hundred genes necessary for viral growth in a cell and nonessential for cellular survival, including the cellular gene comprising SEQ ID NO: 75. Therefore, the gene comprising SEQ ID NO: 75 encodes a gene product that is necessary for viral growth in a cell and nonessential for cellular survival. Since the methods of the present invention resulted in disruption of a gene comprising SEQ ID NO: 75, which resulted in the inhibition of viral infection, it is clear that any compound that results in decreasing or eliminating the gene product and/or the gene product activity of the gene comprising SEQ ID NO: 75 could potentially be effective in treating or preventing a viral infection. In this regard, applicants respectfully remind the Examiner that claim 24 is a screening method directed to identifying compounds that could potentially be involved in treating or preventing viral infection. Thus, it is not necessary to know *a priori* what the relationship between the compound, the gene comprising SEQ ID NO: 75 and the gene product of the gene comprising SEQ ID NO: 75 is. One of skill in the art need only know that the gene comprising SEQ ID NO:75 produces a gene product

necessary for viral growth in a cell and nonessential for cellular survival. It is by utilizing the screening assay as claimed, that one of skill in the art can identify compounds that decrease or eliminate the gene product of the gene comprising SEQ ID NO: 75 and/or the activity of the gene product and thus classify these compounds as potentially effective in treating or preventing viral infection. Once a compound is identified by this screening method, one of skill in the art would know the relationship between the compound, the gene comprising SEQ ID NO: 75 and the gene product, i.e., the compound decreases or eliminates the gene product and/or the activity of the gene product of a gene known to be involved in viral infection. Therefore, as are most compounds identified via screening methods, the compound is a candidate for validation of its effects on viral infection.

With regard to whether SEQ ID NO: 75 is native to the genetic makeup of the cell or a sequence transfected into the cell, applicants point out that the gene comprising SEQ ID NO: 75 can be native to the genetic makeup of the cell or transfected into the cell. Since applicants have already identified a gene comprising SEQ ID NO: 75 as necessary for viral growth in a cell and nonessential for cellular survival, for the screening method of claim 24, it is only necessary to detect the level and/or activity of the gene product in order to identify compounds that could potentially be effective for treating or preventing viral infection. Therefore, the gene comprising SEQ ID NO: 75 can be native to the cell or transfected into a cell because the gene product and the effects of compounds on this gene product are measurable in both instances.

The Office Action states that in claim 30, step d) states that the level of viral infection is "associated" with the cellular gene, but it is allegedly unclear what the association is or how it is made. Step d) of claim 30 is amended herein to recite associating the level of viral infection with the level of the gene product and/or gene product activity of the cellular gene of a), a decrease or elimination of viral infection associated with a decrease or elimination of the gene product and/or gene product activity of a cellular gene of a) indicating a compound effective for treating or preventing the viral infection. Thus, applicants believe that, as amended herein, claim 30 is directed to a method of identifying compounds that decrease or

eliminate viral infection by decreasing or eliminating the gene product and/or the gene product activity of a gene involved in viral infection.

With regard to homologs of SEQ ID NO: 75, as described in the specification (see paragraph bridging pages 9-10), homologs in any desired species, preferably mammalian, such as human, can readily be obtained by screening a human library, genomic or cDNA, with a probe comprising sequences of the nucleic acids set forth in the sequence listing herein, or fragments thereof, and isolating genes specifically hybridizing with the probe under preferably relatively high stringency hybridization conditions. Additionally, the rat sequence can be utilized to devise a probe for a homolog in any specific animal by determining the amino acid sequence for a portion of the rat protein, and selecting a probe with optimized codon usage to encode the amino acid sequence of the homolog in that particular animal. Any isolated gene can be confirmed as the targeted gene by sequencing the gene to determine that it contains the nucleotide sequence listed herein as comprising the gene. Any homolog can be confirmed as a homolog by its functionality. In addition to isolating homologs, one of skill in the art can also search databases with the sequences set forth herein, for example, with SEQ ID NO: 75 to identify homologs of the gene comprising SEQ ID NO: 75. It is standard in the art to perform sequence alignments in order to determine the percent homology between the sequence comprising SEQ ID NO: 75 and its homologs. Therefore, upon identification of a sequence that is a potential homolog of the gene comprising SEQ ID NO: 75, either by isolating a sequence from a library or by database identification, the potential homolog sequence can be tested for its functionality. One of skill in the art would know that if the sequence functions in a similar fashion to the sequence comprising SEQ ID NO: 75, this sequence is a homolog of SEQ ID NO: 75.

Thus, applicants believe that claims 24 and 30 and new claim 31 are clearly defined for one of skill in the art and respectfully request withdrawal of this rejection.

II. Rejection Under 35 U.S.C. § 112, first paragraph

A. The Office Action states that claims 24 and 30 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a nucleic acid homolog of SEQ ID NO: 75. The specification states on page 10 that a nucleic acid homolog is at least 50% homologous to SEQ ID NO: 75, which is 833 nucleotides in length. 50% variation of 833 nucleotides is approximately 416 nucleotides. Therefore, according to the Office Action, the scope of the homolog encompasses sequences that are structurally and functionally unrelated to SEQ ID NO: 75. It is allegedly unclear how a nucleic acid sequence that shares only 50% homology with SEQ ID NO: 75 can be functionally similar to SEQ ID NO: 75 or encodes a product with the required function of reproduction of a virus in a cell, but not necessary for the survival of a cell. Further stated in the Office Action is that the specification does not teach how to structurally modify SEQ ID NO: 75 or how the skilled artisan would readily identify a sequence with the required functions. Therefore, the Office Action concludes that the claims read on nucleic acid sequences with no defined structure, and the specification does not reasonably convey possession of these undefined sequences.

As stated above, it is standard in the art to conduct sequence alignments and identify sequences that have a certain percentage homology with SEQ ID NO: 75. Those sequences identified by one of skill in the art as potential homologs of SEQ ID NO: 75, for example, a sequence that is at least 80% homologous to SEQ ID NO: 75 can be tested in functional assays to determine if the sequence possess the required function of reproduction of a virus in a cell, but is not necessary for the survival of a cell. For example, the sequence for the potential homolog can be disrupted by the methods described in the specification and if its disruption results in a decrease or elimination of viral infection, this sequence is a functional homolog of SEQ ID NO: 75. Again, it is standard in the art to identify sequences that are potentially functionally related to a sequence and confirm that they are, in fact functional homologs. Therefore, applicants believe that by providing the sequence comprising SEQ ID NO: 75 and its function as a sequence necessary for the reproduction of a virus in a cell, but not necessary for the survival of a cell, one of skill in the art would recognize that potential

homologs are a part of the invention. This is because it is so routine to identify homologs and to confirm their functionality such that a screening assay utilizing a homolog of a sequence comprising SEQ ID NO: 75 can be performed to identify compounds that are potentially useful in treating or preventing viral infection. Therefore, there is sufficient teaching in the specification to convey applicants' possession of homologs of SEQ ID NO: 75. Thus applicants believe that claims 24 and 30 are adequately described and respectfully request withdrawal of this rejection.

B. The Office Action states that claims 24 and 30 are rejected under 35 U.S.C.112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a method of screening a compound for the effectiveness in treating or preventing any viral infection by administering a compound to a cell containing a cellular gene comprising SEQ ID NO: 75 or a homolog thereof and a gene product necessary for the production of a virus, contacting the cell with a virus, and correlating the amount of viral infection with the gene product expression to determine the compound's effectiveness in treating or preventing any viral infection.

As discussed above, the Office Action states that it cannot be determined what the relationship is between the compound, the cellular gene, and the gene product. Also, it cannot be determined how the *in vitro* association between the gene product and the compound are associated with *in vivo* amelioration and/or prevention of any viral infection. The specification teaches on page 35, lines 31-33, that SEQ ID NO: 75 has homology to H. sapiens zinc finger transcription factor mRNA. The specification does not teach whether this homology is based on the percentage of sequence identity or evolutionary relationship. A sequence search reveals that SEQ ID NO: 75 is a rat U3 gene trap derived nucleic acid, see the Geneseq sequence alignment provided of SEQ ID NO: 75 with Dubois et al. (WO 99/19481-A2, 7/24/1999, ID NO:AAX57445). SEQ ID NO: 75 also has 53.8% sequence similarity to SEQ ID NO: I encoding 2A5-3 lambda CHO sequence from a Chinese hamster of Morris et al. (US 6,027,915), see the sequence alignment provided. The prior art does not

teach that viral infections are directly linked to association with zinc finger transcription factors, rat U3 gene trap nucleic acids, or nucleic acid sequences from Chinese hamsters. According to the Office Action, there is no teaching in the specification that correlates every viral infection to these genes and the specification does not teach identifying antiviral compounds or how every virus would be susceptible to the compound based on the amount of gene product expressed. Also stated in the Office Action is that the specification does not teach a method of correlating *in vitro* assay data with *in vivo* results and the skilled artisan would doubt that data obtained from an in vitro assay would be immediately applicable *in vivo* or that the results predict the effect on any virus, known and unknown. There are no working examples that demonstrate the association between a cellular gene, and a gene product that is indicative of an antiviral effect. The skilled artisan would not be able to identify a structural and functional homolog of SEQ ID NO: 75 or identify an effective in vivo antiviral compound with the instant method. Therefore, due to the scope of the claims drawn to identifying compounds that are antiviral against any known and unknown viruses, the lack of teaching in the prior art drawn to viral infection and association with zinc finger transcription factors, rat U3 gene trap nucleic acids, or nucleic acid sequences from Chinese hamsters, the lack of teaching and working examples in the specification identifying in vivo antiviral compounds with the instant method, the lack of teaching of how the compound, the gene product, and the cellular genes are associated, the lack of teaching provided for how the skilled artisan would be able to structurally identify a homolog of SEQ ID NO: 75, the Office Action concludes that undue amount of experimentation would be required of the skilled artisan to make and use the invention.

With regard to the relationship between the compound, the cellular gene, and the gene product, as stated above, the gene comprising SEQ ID NO: 75 encodes a gene product that is necessary for viral growth in a cell and nonessential for cellular survival. Thus, it is not necessary to know *a priori* what the relationship between the compound, the gene comprising SEQ ID NO: 75 and the gene product of the gene comprising SEQ ID NO: 75 is. One of skill in the art need only know that the gene comprising SEQ ID NO:75 produces a gene product necessary for viral growth in a cell and nonessential for cellular survival. It is by utilizing the screening assay as claimed, that one of skill in the art can identify

compounds that decrease or eliminate the gene product of the gene comprising SEQ ID NO: 75 and/or the activity of the gene product and thus classify these compounds as potentially effective in treating or preventing viral infection. Once a compound is identified by this screening method, one of skill in the art would know the relationship between the compound, the gene comprising SEQ ID NO: 75 and the gene product, i.e., the compound decreases or eliminates the gene product and/or the activity of the gene product of a gene known to be involved in viral infection. Therefore, as are most compounds identified via screening methods, the compound is a candidate for validation of its effects on viral infection.

The Examiner has stated that it cannot be determined how the *in vitro* association between the gene product and the compound are associated with *in vivo* amelioration and/or prevention of any viral infection. As stated above, applicants respectfully remind the Examiner that claims 24 and 30 are *in vitro* screening methods directed to identifying compounds that could potentially be involved in treating or preventing viral infection. Once a compound is identified by either screening method, or both screening methods, one of skill in the art would know that the compound decreases or eliminates the gene product and/or the activity of the gene product of a gene known to be involved in viral infection (claim 24) or that a compound decreases viral infection *in vitro* by decreasing or eliminating the gene product and/or the activity of the gene product of a gene known to be involved in viral infection (claim 30). Therefore, as are most compounds identified via *in vitro* screening methods, the compound is a candidate for further study and subsequent validation of its effects on viral infection. Therefore, it is not necessary for enablement to correlate the *in vitro* results obtained with the screening assays with how the compound would exert its effects *in vivo* because the purpose of these screening assays is to identify compounds as candidates for further validation of their effects on viral infection based on the compound's ability to decrease or eliminate a gene product and/or a gene product's activity known to be necessary for viral replication but not necessary for survival of the cell. Once one of skill in the art has identified these compounds, their effects can be tested in other cellular assays as well as in *in vivo* animal models to validate their ability to inhibit any type of viral infection. Therefore, the screening assays claimed herein are not directed to the identification of compounds that inhibit viral infection *in vivo*, but instead directed to compounds that, by

virtue of their ability to decrease or eliminate a gene product or a gene product's activity associated with viral infection, are candidates for *in vivo* testing. Since the present invention provides the essential relationship between the gene product and viral infection, this allows identification of compounds potentially effective in treating or prevention of any viral infection that requires this gene product for viral replication.

With regard to the lack of teaching in the prior art drawn to viral infection and association with zinc finger transcription factors, rat U3 gene trap nucleic acids, or nucleic acid sequences from Chinese hamsters, applicants respectfully point out that it is the present invention which first provided evidence of the relationship between SEQ ID NO:75 and viral infection. Therefore, the prior art could not have indicated that SEQ ID NO: 75 or sequences exhibiting homology to SEQ ID NO: 75 are associated with viral infection. Again, it is the present invention that provides this association which is essential for identification of compounds as potential candidates for the treatment or prevention of viral infection via the screening methods of the present invention.

According to the Office Action, the specification does not teach identifying antiviral compounds and does not teach how every virus would be susceptible to the compound based on the amount of gene product expressed. However, this is not required for enablement of the present screening method claims. Applicants respectfully point out that the association between the gene product and viral infection is provided *in vitro* and proof of association *in vivo* is not necessary for enablement of the present screening method claims. Applicants have taught how to identify compounds that decrease or eliminate a gene product or a gene product's activity that is clearly associated with viral infection. Therefore, applicants have provided useful screening methods for the identification of compounds that could potentially treat or prevent any viral infection. It is not necessary to show that a compound identified by the methods of the present invention would treat or prevent any kind of viral infection, but merely to show that a compound that affects a gene product clearly associated with viral infection can be identified such that one of skill in the art can obtain compounds that are promising for further development. Therefore, claims 24 and 30 and new claim 31 are adequately enabled and respectfully request withdrawal of this rejection.

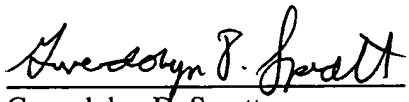
III. New claim 31

New claim 31 is similar to claim 24, with the exception that the method by which a cellular gene comprising the nucleic acid set forth in SEQ ID NO: 75 was identified is included. Support for the enablement and written description of this method of identifying a cellular gene comprising the nucleic acid set forth in SEQ ID NO: 75 can be found in issued U.S. Patent No. 6,448,000, particularly claim 13. Thus applicants believe that new claim 31 is adequately enabled and described.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending claims in this application is believed warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

Payment in the amount of $502.00 ($460.00 extension of time fee and $42 for an independent claim) is to be charged to a credit card and such payment is authorized by the signed, enclosed document entitled Credit Card Payment Form PTO-2038. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,



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Gwendolyn D. Spratt

11-7-02
Date

Marked Up Version of Claim Amendments
Application U.S. Serial No. 09/679,852

30. A method of screening a compound for effectiveness in treating or preventing a viral infection, comprising:

a) administering the compound to a cell containing a cellular gene comprising the nucleic acid set forth in SEQ ID NO: 19, SEQ ID NO: 30, SEQ ID NO: 40, SEQ ID NO: 51, SEQ ID NO; 60, SEQ ID NO: 65, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 109 or SEQ ID NO: 122 or a homolog thereof, and functionally encoding a gene product necessary for reproduction of the virus in the cell but not necessary for survival of the cell;

b) contacting the cell with a virus;

c) detecting the level of viral infection;

d) associating the level of viral infection with the level of the gene product and/or gene product activity of the cellular gene of a), a decrease or elimination of viral infection associated with a decrease or elimination of the gene product and/or gene product activity of a cellular gene of a) indicating a compound effective for treating or preventing the viral infection.